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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/561,324   | 04/19/2006  | Brian A. Kraynack    | CHEM0021USA         | 5906             |
| 32650 7590 08/05/2008<br>WOODCOCK WASHBURN LLP<br>CIRA CENTRE, 12TH FLOOR<br>2929 ARCH STREET<br>PHILADELPHIA, PA 19104-2891 |             |                      |                     |                  |
| EXAMINER   |             |                      |                     |                  |
| VIVLEMORE, TRACY ANN   |             |                      |                     |                  |
| ART UNIT   |             | PAPER NUMBER         |                     |                  |
| 1635   |             |                      |                     |                  |
| MAIL DATE  |             | DELIVERY MODE        |                     |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/561,324

**Applicant(s)**

KRAYNACK ET AL.

**Examiner**

Tracy Vivemore

**Art Unit**

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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3-5-7-9, 14, 20-22, 26, 30, 39-44, 49, 50 and 53-56 is/are pending in the application.
- 4a) Of the above claim(s) 53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3-5-7-9, 14, 20-22, 26, 30, 39-44, 49, 50 and 54-56 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 6/26/06 and 8/1/08.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election of group I, claims 1-52, in the reply filed on May 6, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election of the invention of group I has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election with traverse of the species of 2'-F substituents in the reply filed on May 6, 2008 is acknowledged. The traversal is on the ground(s) that the requirement for election of species effectively requires uniform substitution of oligonucleotides. This is not found persuasive because the instant claims use the open language comprising, which does not preclude the presence of additional substituents. The election of species, which was made for search purposes, does not limit the claims to oligonucleotides having only 2'- fluoro substitutions, but to oligonucleotides having at least one 2'-fluoro substitution. It is noted that the claims as they have been amended are even narrower than the requirement for election of species; requiring at least one 2'-fluoro purine nucleotide be present in the claimed oligonucleotides.

The requirement is still deemed proper and is therefore made FINAL.

Claim 53 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 6, 2008.

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Claims 4, 8, 10-13, 15-19, 23-25, 27-29, 31-38, 45-48, 51 and 52 have been canceled and new claims 54-56 added. Claims 1-3, 5-7, 9, 14, 20-22, 26, 30, 39-44, 49, 50 and 54-56 are pending and examined on the merits.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5-7, 9, 14, 20-22, 26, 30, 39-44, 49, 50 and 54-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fosnaugh et al. (US 2003/0143732).

The claims are directed to compositions of first and second complementary oligomeric compounds wherein one strand is capable of hybridizing to a selected target nucleic acid and wherein one strand comprises 2'

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modified nucleotides having 3'-endo conformational geometry at essentially each position and one of the positions comprises a 2'-fluoro purine nucleotides.

specific embodiments recite which strand comprises the nucleotides having endo conformation, the presence of a stabilizing group such as a dTdT overhang, a 5'-phosphate, a capping moiety such as an inverted deoxy abasic moiety, that both strands have 3'-endo geometry, the identity of the modified nucleotide, the length of the oligomer, and the specific number and identity of the modified nucleotides.

Fosnaugh et al. disclose that short interfering RNAs, duplexes of 21-23 nucleotides that mediate RNA interference, comprise an antisense sequence complementary to a target gene and a sense sequence complementary to the antisense sequence. These siRNAs are useful for a variety of therapeutic, diagnostic, agricultural, target validation, genomic discovery, genetic engineering and pharmacogenomic applications. Chemically-modified siRNAs are expected to improve various properties of siRNAs including increased *in vivo* nuclease resistance and/or improved cellular uptake. Specific embodiments of siRNAs and chemically modified siRNAs are disclosed at pages 3-10. At paragraph 50 Fosnaugh et al. teach that siRNAs can comprise 2'-O-methyl and/or 2'-deoxy-2'-fluoro modifications in the sense strand and the antisense strand and that siRNAs optionally can further comprise a terminal cap molecule at the 3', 5', or both 3' and 5'-ends of the sense or antisense strands. Fosnaugh et al. teach at paragraph 65 that capping moieties include deoxy abasic residues. At paragraph 46 Fosnaugh et al. teach that siRNAs can comprise a 5' phosphate group and at paragraph 68 teach that siRNAs can comprise conjugate groups. Fosnaugh et

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al. teach siRNAs having dTdT overhangs in figure 4 (described at paragraph 145)

While Fosnaugh et al. do not explicitly teach substitution of essentially each of the nucleotides other than 2'-OH as 3'-endo nucleotides or the particular number and pattern of 2'-F and 2'-OMe substitutions recited in the claims, it would be obvious to one of ordinary skill in the art to make siRNAs comprising chemical modifications and because Fosnaugh et al. teach modified siRNAs comprising both 2'-F and 2'-OMe modifications in either the sense or antisense strands without regard to sequence or type of nucleobase and teach that such modifications are desirable to provide increased uptake and nuclease resistance, one of ordinary skill would find it a matter of routine optimization and design choice to predictably produce a siRNA where essentially all positions contain a modification that provides 3' endo conformation. One of ordinary skill in the art would further recognize based on the teachings of Fosnaugh et al. of 5' phosphates, terminal caps, conjugates and overhangs of dTdT nucleotide that inclusion of such moieties is further a matter of design choice in order to provide a siRNA that has the best combination of properties for a particular application.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

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Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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